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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/940,544	09/30/97	SADELAIN M	MSK.P-035-US

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HM12/0918

EXAMINER	
HELMS,L	
ART UNIT	**PAPER NUMBER**
1642	19

DATE MAILED: 09/18/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/940,544	Sadelain et al
Examiner	**Group Art Unit**
Larry R. Helms Ph.D.	1642

☒ Responsive to communication(s) filed on *1 Aug 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-20* is/are pending in the applicat

Of the above, claim(s) *8-20* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-7* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Claims 1-20 are pending.

Claim 1 has been amended.

Claims 8-20 are withdrawn from consideration.

Claims 1-7 are under examination.

2. The text of those sections of title 35, USC Code not included on the Office Action can be found in a prior Office Action.

3. The following Office Action contains some NEW GROUNDS of rejection.

Rejections withdrawn

4. The rejection of claims 1-7 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims and arguments.

5. All rejections of claims 1-7 under 35 U.S.C. 112, first paragraph is withdrawn in view of applicants amendment to the claim.

6. The rejection of claims 1-2 under 35 U.S.C. 102(b) as being anticipated by Alvarez-Vallina et al (Eur. J. Immunol. (1996) 26, pp 2304-2309, Information Disclosure Statement, filed 6/3/98) is withdrawn in view of the new grounds of rejection.

Response to Arguments

Double Patenting

7. The rejection of claims 1-7 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of copending Application No. 09/142974 in view of Alvarez-Vallina et al and Sambrook et al is maintained for the reasons of record.

The response of 8/01/2000 has been carefully considered but is deemed to be not persuasive. The response states that "Applicants will address this rejection, if it maintained, at such time as claims are allowed in both of the applications". The response is not persuasive and the rejection is maintained for reasons of record.

Claim Rejections - 35 USC § 103

8. The rejection of claims 1-7 under 35 U.S.C. 103(a) as being unpatentable over Cheung et al et al (WO 97/34634, published 9/25/97, Information Disclosure Statement filed 6/3/98), and further in view of Alvarez-Villina et al (Eur. J. Immunol. (1996) 26:2304-209, Information Disclosure Statement filed 6/3/98) and Sambrook et al (Molecular Cloning A Laboratory Manual, Cold Spring Harbor Laboratory, 1989) is maintained for the reasons of record.

The response has been carefully considered but is deemed not to be persuasive. The response states the rejection will be obviated with a Declaration Under Rule 131 which will remove the Chung et al reference. However, no such declaration has been submitted and as such the rejection is maintained.

9. The rejection of claims 1-3 under 35 U.S.C. 103(a) as being unpatentable over Cheung et al and further in view of Alvarez-Vallina et al is maintained for reasons of record. The response has been carefully considered but is deemed not to be persuasive. The response states the rejection will be obviated with a Declaration Under Rule 131 which will remove the Cheung et al reference. However, no such declaration has been submitted and as such the rejection is maintained.

The following is a NEW GROUND of rejection.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> > (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> >
> > (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-2 are rejected under 35 U.S.C. 102(a) as being anticipated by Alvarez-Vallina et al (Eur. J. Immunol. (10/1996) 26, pp 2304-2309, Information Disclosure Statement, filed 6/3/98).

a. The claims are drawn to a recombinant polynucleotide encoding a fusion protein comprising a single chain antibody , a signaling domain of human CD28 and a transmembrane

domain wherein the transmembrane domain is disposed between the single-chain antibody and the signaling domain, wherein the transmembrane domain is a human CD28 transmembrane domain.

b. Alvarez-Vallina et al teach chimeric DNA construct containing DNA encoding a single chain antibody fusions with a DNA encoding a truncated CD28 molecule containing the human cytoplasmic signaling domain and transmembrane domain (see page 2305, 3.1). Thus, Alvarez-Vallina et al anticipates the claims.

12. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Eshhar et al (WO 93/19163, published 9/30/93).

a. The claims have been described supra.

b. Eshhar et al teach a fusion protein comprising a single chain antibody and the transmembrane and cytoplasmic domain of CD28 (see page 7 and 8 and pages 18-19).

13. Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eshhar et al (WO 93/19163, published 9/30/93) and further in view of Fouser et al (WO 92/18629).

a. The claims recite a recombinant polynucleotide encoding a fusion protein comprising a single chain anti GD2 antibody an a signaling domain of human CD28 receptor wherein the human CD28 transmembrane domain is disposed between the single chain antibody and the signaling domain.

b. Eshhar et al teach a fusion protein and polynucleotides encoding such for a single chain antibody CD28 fusion (see pages 7-8, 20). Eshhar et al does not teach that the single chain antibody is an anti-GD2 antibody. This deficiency is made up for in the teachings of Fouser et al.

c. Fouser et al teach an anti-GD2 antibody and DNA encoding such. Fouser et al also teach the anti-GD2 antibody can be used synergistically with lymphokines, cytokines, etc, to act more efficiently to kill the targeted tumor cells (see page 7).

d. It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the anti-GD2 antibody of Fouser and produce a anti-GD2 fusion protein with the human CD28 receptor as taught by Eshhar et al.

e. One of ordinary skill in the art would have been motivated to used the have used the anti-GD2 antibody of Fouser and produce a anti-GD2 fusion protein with the human CD28 receptor as taught by Eshhar et al because Eshhar et al teach "the ScFv portion of the present invention may be any antibody, the specificity of which is desired" (see page 20). In addition, one of ordinary skill in the art would have been motivated to used the have used the anti-GD2 antibody of Fouser and produce a anti-GD2 fusion protein with the human CD28 receptor as taught by Eshhar et al because Fouser et al teach "The 3F8-type antibodies of the present invention mediate the in vitro cytotoxicity of the target cells that express the GD2 antigen on the surface (see page 5). In addition, one of ordinary skill in the art would have been motivated to used the have used the anti-GD2 antibody of Fouser and produce a anti-GD2 fusion protein with the human CD28 receptor as taught by Eshhar et al because one skilled in the art would know In

vitro studies have shown that monoclonal antibodies against gangliosides like GD2 and GD3 potentiate lymphocyte response which could potentially be directed towards tumor cells.

f. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

13. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eshhar et al (WO 93/19163, published 9/30/93) and further in view of Fouser et al (WO 92/18629, published 10/29/92) and Sambrook et al (Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, 1989).

a. Claims 1-3 have been described supra. Claims 4-7 recite a recombinant polynucleotide further comprising thymidine kinase.

b. Eshhar et al and Fouser et al have been described supra. Eshhar et al does not teach the anti-GD2 antibody or the thymidine kinase. These deficiencies are made up for in the teachings of Fouser and Sambrook et al.

c. Sambrook et al teach the thymidine kinase gene, which is expressed in most mammalian cells (Page 16.9). Sambrook et al also teach a plasmid, pTK2, which carries a fragment of the herpes simplex virus (HSV) encoding thymidine kinase (tk) (see page 16.11, Figure 16.1A).

d. It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to produce a polynucleotide encoding a fusion protein

comprising a single chain anti-GD2 antibody and a signaling domain of human CD28 and human CD 28 transmembrane domain and a gene coding for thymidine kinase.

e. One of ordinary skill in the art would have been motivated to produce a polynucleotide encoding a fusion protein comprising a single chain anti-GD2 antibody and a signaling domain of human CD28 and human CD 28 transmembrane domain and a gene coding for thymidine kinase because of reasons given above in the Eshhar et al and Fouser et al 103 rejection and further because Sambrook et al teach a medium containing hypoxanthine, aminopterin, and thymidine (HAT medium) "in which only cells expressing the tk gene will grow. Thus, by using the appropriate medium it is therefore possible to select for cells expressing the tk gene". Thus, it would have been obvious to combine the teaching of Eshhar et al and Fouser for producing a polynucleotide encoding for a fusion protein of a single chain anti-GD2 antibody and the signaling and transmembrane domains of CD28 and further combine this polynucleotide with a polynucleotide encoding the thymidine kinase protein of Sambrook et al for selection of cells expressing the polypeptide.

f. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art a the time the invention was made, as evidenced by the references.

Double Patenting

14. Claims 1-7 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of copending Application No. 09/142974 in view of Eshhar et al (WO 93/19163, published 9/30/93), Fouser et al (WO 92/18629, published 10/29/92) and Sambrook et al (Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, 1989).

a. The claims in the present and copending application are each drawn to a recombinant polynucleotide encoding a fusion protein comprising the variable region of the light chain of the anti-G_{D2} antibody linked to the variable region of the heavy chain of the anti-G_{D2} antibody further comprising a region encoding for an additional protein.

b. The claims in application 09/142974 are broader in scope that those of claims 1-7 in the instant application. Claims 1 and 2 in application 09/142974 are drawn to a recombinant single chain polynucleotide comprising a region encoding the variable region of the light and heavy chain of an anti-G_{D2} antibody and a region encoding an additional protein.

c. It would have been obvious to use the DNA encoding an additional fusion protein of human CD28 comprising the signaling domain and the transmembrane domain as well as add a DNA encoding for the thymidine kinase protein as recited in the present application for reasons cited above in the 103 rejection with Fouser et al and Eshhar et al and further because Sambrook et al teach the thymidine kinase gene, which is expressed in most mammalian cells (Page 16.9). Sambrook et al also teach a plasmid, pTK2, which carries a fragment of the herpes simplex virus (HSV) encoding thymidine kinase (tk) (see page 16.11, Figure 16.1A) and Sambrook et al teach a medium containing hypoxanthine, aminopterin, and thymidine (HAT medium) "in which only

cells expressing the tk gene will grow. Thus, by using the appropriate medium it is therefore possible to select for cells expressing the tk gene".

Accordingly, the claimed polynucleotide encoding a fusion protein in the copending application and the present application are obvious variants.

Therefore, the inventions as claimed are co-extensive.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusions

15. No Claims are allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

17. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal

Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Respectfully,

SHEELA HUFF
PRIMARY EXAMINER

Larry R. Helms Ph.D.

703-306-5879